## REMARKS

The Office Action dated February 27, 2007, has been carefully reviewed and the following comments are made in response thereto. In view of the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Claims 25, 26, and 28 have been amended to be directed to methods of treatment in a human. Exemplary support for the amendments is found on page 14, lines 24 to 25, page 15, lines 8 to 14, page 17, lines 13 to 20, page 18, lines 10 to 11 and page 38, lines 15 to 25 of the specification. No new matter has been added by these amendments.

**The Rejections under 35 U.S.C. 112, first paragraph should be withdrawn**

Claims 25, 26, and 28 were rejected under 35 U.S.C. 112, first paragraph for allegedly failing to comply with the written description requirement. Claims 25, 26, and 28 were also rejected under 35 U.S.C. 112, first paragraph for lack of enablement.

Claims 25, 26, and 28 allegedly fail to provide sufficient distinguishing characteristics for the claimed genus of anti-CXR4 antibodies or fragment thereof, and anti-SDF-1 antibody or fragment thereof. Therefore, these claims are alleged to not comply with the written description requirement.

As the Examiner is aware, "as long as an applicant has a '*fully characterized* antigen' by its structure, formula, chemical name, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen." *Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2003) (emphasis in original). As the Examiner noted, the specification discloses human CXCR4 (SEQ ID NO: 1) (page 14, lines 24 to 26) as well as the two types of human SDF-1: (1) human SDF-1α (SEQ ID NO: 5) and (2) human SDF-1β (SED ID NO: 9) (page 15, lines 8 to 14). The specification also discloses both the amino acid and nucleotide sequence of human CXCR4 and human SDF-1 (page 15, lines 1 to 20). Furthermore, the specification describes (1) that both SDF-1 and CXCR4 are necessary for neovascularization, (2) known structural of details of CXCR4 such as *e.g.*, that CXCR4 is a seven-transmembrane spanning G-protein coupled protein and a receptor for SDF-1 and (3) the role of SDF-1 (page 2, line 20 to page 4, line 10).

The specification also discloses anti-SDF-1 antibodies (page 17, lines 13 to 20) and anti-CXCR4 antibodies (page 18, lines 10 to 11). The specification discusses in detail how to make such antibodies (page 26, line 25 to page 32, line 36). The specification further discloses methods of treating cancer, treating a pathology caused by neovascularization and suppressing vascularization with such antibodies (*see* page 38, lines 15 to 25). As amended claims 25, 26, and 28 are directed to methods of treating cancer or suppression of neovascularization in a subject by administration of anti-human SDF-1 antibodies or anti-human CXCR4 antibodies. Each of the elements of these claims is disclosed in the specification, one of skill in the art would recognize what is claimed in sufficient detail to reasonably conclude that the inventors were in possession of the claimed invention. Therefore, as amended, claims 25, 26 and 28 comply with the written description requirement.

Claims 25, 26, and 28 are rejected under 35 U.S.C. 112 first paragraph for lack of enablement. As the Examiner is aware, "[t]he test for enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation" *In Wands*, 858 F.2d 721, 737 (Fed. Cir. 1988). To facilitate the analysis *In re Wands* set forth several factors to determine what undue experimentation is. Rather than discussing each of the factors on its own, Applicants have combined the analysis. Based on that analysis, Applicants respectfully submit that the claims as amended are enabled.

As discussed, the claims, as amended, are directed to methods of treating cancer or suppressing neovascularization by administration of anti-human SDF-1 antibodies or anti-human CXCR4 antibodies, which inhibit the binding between CXCR4 and SDF-1. Furthermore, as discussed, the specification discloses the sequence of human CXCR4 and human SDF-1 (SDF-1$\alpha$ and SDF-1$\beta$) and methods of making antibodies.

At the time of filing, both SDF-1 and CXCR4 were known proteins. Applicants conducted a variety of experiments and determined that CXCR4 is essential for neovascularization (*see e.g.*, page 3, lines 3 to 5). Applicants showed for example that CXCR4 and SDF-1 are essential to neovascularization (page 52, lines 21 to 26) and that CXRC4 is a primary receptor for SDF-1 (*see* page 53, lines 8 to 10). Thus, Applicants clearly demonstrated the connection between neovascularization and CXCR4 and SDF-1.

Since CXCR4 is a primary receptor of SDF-1, it is clearly well within skill in the art, without undue experimentation, to inhibit the interaction between CXCR4 and SDF-1 with an agent that inhibits

the receptor-ligand binding. It also well known that antibodies can be used to inhibit receptor ligand binding. In addition, it is well within skill in the art, without undue experimentation, how to obtain such antibodies (*see* M.P.E.P. 2164.06 (Time and difficulty are not determinative if they are merely routine)). To facilitate obtaining such antibodies, the specification discloses numerous methods of isolating and making such antibodies as well as various types of suitable antibodies (*see* page 26, line 25 to page 32, line 26).

It is well known that neovascularization is crucial to the proliferation of solid tumors (*see* page 1, lines 19 to 21). Inhibitors of neovascularization are thus used for cancer treatment (*see* page 1, line 22 to page 2, line 4). As discussed, Applicants demonstrated the connection between neovascularization, the receptor CXCR4 and its ligand SDF-1. The specification even discloses a mechanism of action by which these inhibitors are effective in treating cancer (page 6, lines 11 to 17 ("Because the formation of median or large arterioveins is essential for the maintenance and enlargement of a cancer tissue that exceeds a certain size, the vascularization inhibitor...blocks the CXCR4 or SDF-1 signaling system, thus suppressing the maintenance and enlargement of cancer tissue")). In addition, the specification discloses that use of CXCR4 inhibitors "allows for the inhibition of vascularization; therefore, it will exert an antitumor effect (inhibition of neovascularization) on solid cancer in addition to antitumor effects on angiosarcoma (cancer of blood vessels themselves) and Kaposi's sarcoma" (*see* page 38, lines 15 to 23). It will also exert therapeutic effects against diseases pathologically caused by neovascularization, such as chronic articular rheumatism, psoriasis, and diabetic retinopathy (*see* page 38, lines 23 to 25). The specification also clearly teaches methods of treating cancer and suppression of neovascularization with CXRC4 and SDF-1 inhibitors such as *e.g.*, anti-human SDF-1 antibodies and anti-human CXCR4 antibodies (*see* page 38, lines 15 to 25). The specification also discloses use of assays to prove that the methods of the invention are effective (*see* page 39, line 10 to page 40, line 15). Therefore, one of skill in the art would be able to administer antibodies according to the invention to prevent vascularization, including, but not limited, to cancer or a pathology associated with neovascularization. Applicants respectfully submit that numerous references, including those cited by the Examiner, support the proposition that one of skill in the art would be able to administer anti-human SDF-1 antibodies and anti-human CXCR4 antibodies for the treatment of cancer and suppression of neovascularization without undue experimentation. *See e.g.*, Seghal *et al.* (1998) J. Surgical. Oncol. 69(2): 99-104 (CXCR4 required for proliferation of glioblastoma cells); Moehle *et al.* (1998), Blood 91(12): 4523-4530 (CXCR4 may be involved in trafficking of malignant hematopoietic cells).

Furthermore, as the Examiner is aware compliance with the enablement requirement does not turn on whether an example is disclosed (*see* M.P.E.P. 2164.02). An applicant need not have actually reduced the invention to practice prior to filing. *Gould v. Quigg,* 822 F.2d 1074, 1078 (Fed. Cir. 1987). In addition, the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without undue experimentation. *In re Borkowski,* 422 F.2d 904, 908 (CCPA 1970). As discussed above, the application provides sufficient teaching throughout the specification to enable the skilled artisan to practice the claimed invention without undue experimentation. Thus, claims 25, 26, and 28 are clearly enabled.

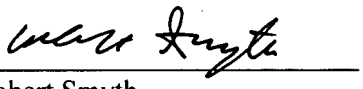
In light of the foregoing arguments and amendments, Applicants respectfully request withdrawal of the rejections of claims 25, 26, and 28 under 35 U.S.C. 112, first paragraph.

**Conclusion**

It is respectfully submitted that all claims are now in condition for allowance, early notice of which would be appreciated. Should the Examiner disagree, Applicants respectfully request a telephonic or in-person interview with the undersigned attorney to discuss any remaining issues and to expedite the eventual allowance of the claims.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
**Morgan, Lewis & Bockius LLP**



Robert Smyth
Registration No. 50,801

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Morgan, Lewis & Bockius LLP
Customer No. **09629**
1111 Pennsylvania Avenue, N.W.
Washington, D.C. 20004
202-739-3000